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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,860	01/16/2004	Wei Wang	DX0589K1D	1271

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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
KEMMERER, ELIZABETH	
ART UNIT	PAPER NUMBER
1646	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/759,860	WANG ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15,16,18,19 and 22-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,15,16,18,19,22-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of the species of (a) macrophages, (h) inflammatory response in the gastrointestinal tract, including colon and small intestines, and (d) antagonist that is an antibody in the reply filed on 08 January 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Status of Application, Amendments, And/Or Claims

The preliminary amendment of 25 January 2007 has been entered in full. Claims 2-14, 17, 20, and 21 are canceled. Claims 1, 15, 16, 18, 19, and 22-31 are under examination as they are directed to the elected species.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 15, 16, 18, 19, and 22-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of claim 1 recites treatment of a disease in a subject. However, the method step recites contacting a cell with an antibody, which reads on *in vitro*

methods. The method step does not achieve the goal set forth in the preamble. Therefore, it is unclear whether the claimed method is directed to a method of treating a subject, or a more broad method of contacting a cell *in vitro* or *in vivo*. Recitation of a step directed to administration of the antibody to a patient suffering from inflammation of the gastrointestinal tract is suggested.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 15 is directed to a method of treating an inflammatory response in the colon of a subject comprising use of an antagonistic antibody of a TECK polypeptide comprising the sequence set forth in Gln1 to Leu127 of SEQ ID NO: 4.

The specification teaches the following:

> Four independent lines of transgenic mice expressing TECK in the brain have been made. All animals had neurologic disorders. In addition, several of them suffered severe infections. The consequences of TECK could be a direct one on brain cells which nature remains to be identify. Alternatively, since TECK has been shown in vitro to have effects on macrophages and dendritic cells which are critical effectors of immune responses, the overproduction of TECK could lead to distant effects on these cells at sites of infection. These results suggest that the blockade

> of TECK production in vivo may help to resolve particular pathological processes, in particular infections. The localization suggests a physiological role in immunological responses involving the thymus, or in colon/small intestine or gastrointestinal inflammation, e.g., Crohn's disease or inflammatory bowel disease.

It is noted that originally filed claims encompassed antagonistic antibody therapy for inflammatory diseases of the gastrointestinal tract, including the colon.

The application fails to provide an enabling disclosure for the claimed method for the following reasons.

The specification and originally filed claims merely assert that an anti-TECK antibody would be effective in treating inflammation of the colon. There are no working examples, nor any clear guidance that such a therapeutic approach would be efficacious.

The literature indicates that TECK (also known as CCL25) is expressed in the small intestine, especially inflamed small intestine, but not in normal or inflamed colon. Furthermore, the literature indicates that peripheral blood lymphocytes expressing the TECK receptor, CCR9, are highly elevated in patients suffering from small bowel Crohn's disease or celiac disease, but not in patients suffering from purely colonic Crohn's. See Papadakis et al. (2001, Gastroenterology 121 :246-254). The literature also indicates that TECK (CCL25) expression remains restricted to the small intestine in patients with ileitis. See Rivera-Nieves et al. (2006, Gastroenterology 131:1518-1529). Rivera-Nieves et al. further disclose that neutralization of the receptor or chemokine with an antagonistic antibody attenuated early ileitis. Hosoe et al. (2004, Am. J. Physiol. Gastrointest. Liver Physiol. 286:G458-466) showed that anti-TECK antibodies

attenuated the TNF-α-induced lamina proprial lymphocyte adhesion in the small intestine but not in the colon. Hosoe et al. conclude that TECK may play an important role in the adherence of mucosal lymphocytes to the microvessels of the small intestine but not the colon under uninflamed as well as inflamed conditions. Finally, Hieshima et al. (2004, J. Immunol., 173:3668-3675) further support the findings that TECK (CCL25) plays a role in small intestine but not in colon.

The only publication that was found that supports the claimed invention is an abstract by Wei et al. (2005, Gastroenterology 128 (4 Suppl. 2): A-204 to A-205), which includes inventor Thomas Schall as one of the authors. The abstract reports that a small molecule inhibitor of CCR-9 mediated chemotaxis had a positive effect on a model of small intestine Crohn's disease and a model of ulcerative colitis. However, this result is not commensurate in scope with the claims, which recites an antagonistic antibody of TECK, not a small molecule inhibitor of its receptor. Furthermore, as this is a single abstract which is devoid of experimental detail, it does not effectively counterbalance the evidence in the literature (reviewed in the preceding paragraph) that TECK does not play a role in inflammation of the colon. The preponderance of the totality of the evidence indicates that an anti-TECK antibody would have no effect on inflammation of the colon.

Finally, it is noted that, due to the recitation of the word "comprising," claim 15 does not specify that the antibody must bind an epitope within the recited sequence of Gln1 to Leu127 of SEQ ID NO: 4. Therefore, the claim is very broad in that it recites an antibody that has a required function (i.e., antagonistic activity on TECK), but no

meaningful structural limitation. Amending the claim to require that the antibody bind an epitope within Gln1 to Leu127 of SEQ ID NO: 4 would resolve this issue.

Due to the large quantity of experimentation necessary to empirically determine how to treat colon inflammation with anti-TECK antibodies, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the contradictory state of the prior art, the unpredictability of the effects of untested drugs, and the breadth of the claim, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

If Applicant is aware of any publication or other evidence that can be submitted in the form of a declaration under 37 C.F.R. § 1.132 regarding the effects of anti-TECK antibodies on inflammation of the colon, such would be considered probative of this issue.

Claims 1, 16, 18, 19, and 22-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for treating an inflammatory response in the small intestine of a subject comprising administering an antagonistic antibody or an antigen-binding fragment thereof that binds specifically to an epitope located within Gln1 to Leu127 of SEQ ID NO: 4, does not reasonably provide enablement for treatment of other inflammatory responses or for treatment using an anti-TECK antibody that does not bind an epitope with Gln1 to Leu127 of SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are directed to methods of treating an inflammatory response in the gastrointestinal tract of a subject using an antagonistic antibody or an antigen-binding fragment thereof that binds specifically to a TECK polypeptide comprising the amino acid sequence of Gln1 to Leu127 of SEQ ID NO: 4.

The teachings of the specification, original claims, and relevant literature are discussed above. For the same reasons as discussed above, the claimed methods are not enabled for treating inflammatory responses in the gastrointestinal tract other than those of the small intestine. Examples of enabled diseases include Crohn's disease of the small intestine and inflammatory bowel disease of the small intestine. Examples of non-enabled diseases include colitis.

Similarly, for the reasons discussed above, use of antagonistic antibodies (or fragments thereof) which do not bind an epitope located within Gln1 to Leu127 of SEQ ID NO: 4 are not enabled.

Due to the large quantity of experimentation necessary to empirically determine how to treat gastrointestinal inflammation other than small intestine inflammation with anti-TECK antibodies, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the contradictory state of the prior art, the unpredictability of the effects of untested drugs, and the breadth of the claim, undue

experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Conclusion

The claims are free of the prior art. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (571) 272-0874. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D. can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elizabeth C. Kemmerer

ECK

ELIZABETH KEMMERER
PRIMARY EXAMINER